

REMARKS

Claims 1-16 were in the application as originally filed. Claim 3 was cancelled and Claims 15-18 were added in the Amendment filed on October 16, 2002. Claims 19-22 were added in the amendment filed on January 21, 2004. Claims 1-2 and 4-22 are currently pending.

Claims 1 and 2 have been amended in order to indicate that the helium in the milling fluid is in a gaseous state. Support for these amendments can be found, for example, on page 4, lines 22-26, and page 5, lines 8-10, of the specification.

Applicants note with appreciation that the rejection of claims 12 and 13 under 35 U.S.C. § 102(b) as being anticipated by Jinks et al. and the rejection of claims 12 and 13 under 35 U.S.C. § 103(a) as being unpatentable over Jinks et al. have been withdrawn.

Claims 1-2 and 4-22 are rejected under 35 U.S.C. § 103(a) as, the Examiner asserts, being unpatentable over Weishaupt et al. (U.S. Patent No. 3,897,010), in view of Hagan et al. (U.S. Patent No. 4,767,612) alone, or further in view of Capelle, Jr. et al. (U.S. Patent No. 6,145,765) apparently for the reasons set forth in the Office Action dated February 27, 2004, on the grounds that the Weishaupt reference allegedly teaches a method of milling material wherein a fluid energy mill is employed to micronize the material wherein the fluid is an inert gas at a low temperature, the temperature of the fluid lies in a cryogenic range or in a range of the liquefaction temperatures of the inert gas used in the method, the purpose of the low temperature is to embrittle the milling material to facilitate pulverization, and the temperature of the fluid is reduced to a point such that the material to be milled is no longer plastically or elastically viscous but ruptures readily upon impact with a surface or another particle.

The Examiner acknowledges that Weishaupt et al. do not expressly teach that the material to be milled is triamcinolone acetonide or the inert gas to be helium. The Examiner, therefore, relies on the secondary Hagan et al. reference for teaching the micronization of triamcinolone acetonide in a fluid energy mill and a particle size range of from 1 to 5 microns for micronized triamcinolone acetonide. The Examiner concludes that at the time the invention was made, it would have been obvious to a person of ordinary skill in the art to mill triamcinolone acetonide in a fluid energy mill

at low temperatures to a mean particle size of 2 microns because one would have been motivated to provide a method that embrittles the milled material to be comminuted.

Lastly, the Examiner maintains that Capelle, Jr. et al. teach that the inert gas used as the fluid for a fluid energy mill can be helium, and concludes that it would have been obvious to a person of ordinary skill in the art to incorporate helium as the fluid in the fluid energy mill because one would have been motivated to choose a gas that is compatible with the material being processed and which does not degrade the material upon contact with the fluid.

This rejection is traversed and reconsideration and withdrawal thereof are respectfully requested for the reasons given hereinbelow.

The instant invention is generally directed to *crystalline materials* containing substantially no amorphous content having a median particle size of less than 10 microns and to methods for producing *fine, highly crystalline material products* by fluid energy milling a crystalline material using a low temperature (between -30°C and -120°C) milling fluid comprising *helium gas*. Applicants' invention overcomes the problem of high amorphous material content found in materials subsequent to fluid energy milling (specification, p1, lines 14-16; p. 2, lines 2-3). In contrast, the primary reference cited by the Examiner, Weishaupt et al. is directed to a milling system wherein a gas is compressed and then cooled prior to introduction into a fluid-energy mill, where the fluid is expanded to comminute solid materials, especially materials of high plastic deformability, especially synthetic resins (col. 2). As the Examiner has acknowledged, Weishaupt et al. fail to disclose the use of helium as a milling fluid. However, the Examiner contends that Weishaupt et al. *implicitly* teach use of an inert gas, which includes helium. Nevertheless, the only milling fluids actually disclosed by Weishaupt et al. are *liquefied* argon, nitrogen, and, oxygen. Moreover, Weishaupt et al. consistently refer to the use of *liquefied* fluids in their milling process (see e.g. col. 7, lines 8-19) as opposed to gas-containing fluids as *required* by the present invention, and clearly do not teach or suggest the use of gaseous helium at reduced, yet non-cryogenic temperatures.

The second reference cited by the Examiner, Hagan et al., discloses triamcinolone acetone micronized in a fluid energy mill until 90-95% by weight was in the particle size range of 1 to 5

microns (col. 2). Nowhere in the cited patent, however, is there a disclosure of a highly crystalline material or a process for preparing a fine, highly crystalline material utilizing a milling fluid containing helium gas at temperatures between -30°C and -120°C , all aspects *required* by Applicants' claimed invention. The Examiner, nevertheless, concludes that in view of the Weishaupt et al. and Hagan et al. references, the invention as a whole would have been *prima facie* obvious to one skilled in the art at the time the invention was made. Applicants disagree.

The stated purpose for using low temperature fluids according to the Weishaupt process is to embrittle the milling material to facilitate pulverization. Nowhere in the cited references is there a teaching or suggestion that fine, highly crystalline material *can* be prepared by fluid energy milling a crystalline material using milling fluids at reduced temperatures. Despite this lack of disclosure, the Examiner suggests that one skilled in the art would have otherwise been motivated to mill triamcinolone acetonide in a fluid mill at low temperatures to a mean particle size of 2 microns so as to embrittle the milled material to be comminuted in order to increase efficiency of the process. Even assuming *arguendo* that such a motivation to combine the teachings of Weishaupt et al. and Hagan et al. exists, it is irrelevant because Applicants have shown that milling a crystalline material such as triamcinolone acetonide in a fluid mill at low temperatures does not necessarily produce a fine, highly crystalline material product, as is provided by Applicants' claimed process. Specifically, Applicants have indicated that common milling fluids such as nitrogen and air become less effective as their temperatures drop (specification p. 3, lines 7-10). Additionally, Applicants have illustrated that the use of low temperature nitrogen for milling triamcinolone acetonide resulted in a relatively high amorphous content (specification, p. 4-5). Since the only motivation to choose a milling fluid that would allow for the production of a highly crystalline material comes from the teachings contained in Applicants' own disclosure, it is submitted that it is only through impermissible hindsight that one skilled in the art would choose low temperature *helium gas* over those fluids *actually* disclosed in Weishaupt. Thus, in view of the above-described superiority of Applicants' milling fluid containing low temperature helium gas over the milling fluids actually described by Weishaupt, the lack of disclosure of highly crystalline materials such as highly crystalline triamcinolone acetonide in *either* reference, and the failure of a suggestion or a teaching that such fine, highly crystalline materials can be prepared using a fluid energy mill, Weishaupt et al. and Hagan et al., either alone, or in combination, are inadequate to render obvious the present invention.

Apparently recognizing the above-mentioned deficiencies in the primary Weishaupt et al. and Hagan et al. references, the Examiner next relies on the Capelle patent for the proposition that helium can be utilized in energy milling. The Capelle, Jr. patent discloses a fluid energy mill of a vortex type for comminuting pulverulent materials, such as pigments. Capelle, Jr. et al. note that any carrier gas can be used as the fluid, such as nitrogen, compressed air, helium, steam, CO₂, steam under pressure, and superheated steam, or other vapors or gases based on their compatibility with the material being processed and provided the materials involved are not degraded by contact with the carrier gas. However, the Capelle reference *fails* to teach or suggest the use of a milling fluid containing helium at *reduced temperatures*, as is *required* by the instant invention. Moreover, Capelle, Jr. et al. do not teach the use of helium, or any other carrier gas for that matter, to obtain a *fine, highly crystalline material* product. Thus, at most, the Capelle, Jr. reference cited by the Examiner might make it obvious to try using helium in general as a milling fluid. However, it is well settled that "obvious to try" is not the standard against which obviousness is measured under 35 U.S.C. § 103. *In re Goodwin* 198 USPQ 1; *In re Antonie* 195 USPQ 6.

Lastly, in response to Applicants' previous remarks filed July 27, 2004, the Examiner relies on *In re McLaughlin* (170 USPQ 209) for the proposition that so long as any judgment on obviousness takes into account *only* knowledge which was within the level of ordinary skill at the time the claimed invention was made, and *does not* include knowledge gleaned only from the applicant's disclosure, hindsight reconstruction is proper. However, for the reasons given hereinabove, it is *only* in view of the teachings in Applicants' disclosure and the described inadequacies of other milling fluids that one skilled in the art would choose low temperature milling fluids containing helium gas to prepare fine, highly crystalline materials. Hence, *In re McLaughlin* is improperly applied to the case at bar.

In conclusion, *none* of the references cited by the Examiner disclose highly crystalline materials having a mean particle size of less than 10 microns, less than 2 microns, or about 1 micron; or crystalline materials with amorphous content of less than 5%, 2%, or 1%; all of which are different aspects of the invention embraced by the present claims. Nor do any of the cited references teach or suggest any processes for preparing fine, highly crystalline materials, nor the use of a low temperature milling fluid containing helium gas in such a process. Finally, none of the

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cited references, either alone or in combination, describe crystalline triamcinolone acetonide containing substantially no amorphous content and having a mean particle size of less than 2 microns, as required by instant claim 14.


In view of the foregoing, Applicants submit that none of the cited references taken alone or in combination are competent to render Applicants' claimed process obvious. Moreover, none of the references has any teaching or suggestion which would have led a person of ordinary skill in the art to Applicants' claimed fine, highly crystalline material. The claimed invention would, therefore, not have been obvious to such a person at the time the invention was made and, hence, the rejection of the claims 1-2 and 4-22 under 35 U.S.C. §103(a) based on said references is believed to be unwarranted and should be withdrawn.

There being no remaining issues, this application is believed to be in condition for favorable reconsideration and early allowance and such actions are respectfully requested.

The Commissioner is hereby authorized to charge any additional fees which may be required by this paper, or credit any overpayment to Deposit Account No. 18-1982.

Respectfully submitted,

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Kelly L. Bender
Reg. No. 52,610

sanofi-aventis
Patent Department
Route 202-206; Mail Code: D-303A
Bridgewater, NJ 08807
Facsimile: (908) 231-2626
Telephone: (610) 889-8995